



## Chlamydia-related bacteria

***Studying the prevalence and pathogenesis of novel Chlamydia-related organisms in UK cattle (BBSRC IPA Project BB/J015083/1).***

In recent years, there has been an increase in the identification of a group of emerging bacterial organisms found in the environment and shown to be associated with a variety of conditions in humans, such as pneumonia and miscarriage. These organisms, which share similar biological characteristics to traditional chlamydia species, are referred to as Chlamydia-like/related organisms. These organisms are also increasingly becoming recognized as potential disease causing organisms of livestock, being particularly associated with the pre-natal death of calves. Indeed, they have been found in over a quarter of the cases analysed in the UK, and thus could account for some of the 80% unaccounted, undiagnosed cases reported by DEFRA.

To date, studies have relied upon the analysis of tissue samples that have been submitted to veterinary laboratories for disease diagnosis. While these studies have been vital in demonstrating the presence of the organisms in samples for which no alternative diagnoses could be reached, they have been performed on a relatively small number of samples. In addition, in general, little information has been obtained on the disease and production histories of the farms from which the animals originated. Therefore, joint funding has been obtained from the BBSRC and Zoetis (BBSRC IPA Project '*Emerging Chlamydia-like organisms as novel causes of bovine reproductive failure*' (BB/J015083/1)) to investigate the epidemiology of Chlamydia-related species in UK cattle, their association with cattle reproductive performance, placental lesion development and abortion, as well as investigating at a molecular level the basis for pathogenesis using novel in vitro and in vivo model systems. The project is in collaboration with Professor Javier Guitian at the Royal Veterinary College, London and Dr Duncan Mwangi at Zoetis, Kalamazoo, US.

### Specific project aims and objectives:

1. Epidemiological studies to determine the prevalence of Chlamydia-related organisms (and other common abortifacients) at the farm level, potential causal association of organisms with reproductive failure and environmental contamination.
  - Objective 1a: Cross-sectional study in association with a DairyCo to determine the prevalence of key diseases and conditions (Neospora caninum, Salmonella, Leptospira, BVDV, BHV-1 and Chlamydia-related organisms) among UK dairy herds and levels of milk production and reproductive efficiency.
  - Objective 1b: Enrol and monitor cohort study from selected farms for reproductive performance to investigate any potential causal association with the presence of Chlamydia-related organisms. These studies will enable the determination of the prevalence of these organisms and how their presence affects the reproductive performance on a farm basis.
  - Objective 1c: Analyse environmental samples for the presence of live organisms, as a potential route for transmission.
2. An association between Chlamydia-related organisms and abortion has previously been demonstrated, however, there has been little characterisation of the organisms present within the tissues and lesions.
  - Objective 2a: Investigate the relationship between the presence of the organism with respect to placental lesion development using archived and prospectively collected samples to determine any association with reproductive performance.

- Objective 2b: Molecular phylogenetic analysis of 16S rRNA gene sequences to determine diversity and similarity with known species.
  - Objective 2c: Isolation and growth of novel Chlamydia-related organisms from clinical and environmental samples using amoebal co-culture techniques.
3. Pathogenic effects of bacterial infections in the host are generally elicited, either directly or indirectly, through the effects of the immune response mounted in response to that infection. Complementary in vitro and in vivo models of infection will be established to understand the sequence of events that lead to pathogenesis within target tissues following infection with Chlamydia-related organisms *Parachlamydia acanthamoeba* and *Waddlia chondrophila*.
- Objective 3a: Develop an in vitro model of placental infection utilizing a ruminant trophoblast cell line.
  - Objective 3b: Develop an in vivo model in cattle to demonstrate the disease causing potential of these organisms in the host species.

The combination of these studies will greatly increase our understanding of the disease causing potential and role of this group of emerging bacteria in cattle reproduction and mechanisms of immunopathogenesis that result in reproductive failure. The outcomes will lead to improved diagnoses of cattle reproductive failure, inform and educate the industry to the presence of these organisms, lead to improved management systems and allow an evaluation of the potential benefits of future vaccine strategies to prevent disease incidence.

#### **Selected publications:**

Wheelhouse, N., Mearns, R., Willoughby, K., Wright, E., Turnbull, D. and Longbottom, D. (2015). Evidence of *Chlamydia*-related organisms in bovine abortions in England and Wales. *Veterinary Record* 176, 18.

Wheelhouse, N. and Longbottom, D. (2015). *Chlamydia*-related organisms: Infection in ruminants and potential for zoonotic transmission. *Current Clinical Microbiology Reports* 2, 1–9.

Wheelhouse, N., Coyle, C., Barlow, P., Mitchell, S., Greub, G., Baszler, T., Rae, M. and Longbottom, D. (2014). *Waddlia chondrophila* infects and multiplies in ovine trophoblast cells stimulating an inflammatory immune response. *PLoS ONE* 9(7):e102386.

Wheelhouse, N., Longbottom, D. and O'Donovan, J. (2014). *Chlamydia* in cases of bovine abortion in Ireland. *The Veterinary Journal* 174, 560-1.

Wheelhouse, N., Howie, F., Gidlow, J., Greub, G., Dagleish, M. and Longbottom, D. (2012). Involvement of *Parachlamydia* in bovine abortions in Scotland. *Veterinary Journal* 193, 586-8.

Wheelhouse, N. and Longbottom, D. (2012). Endemic and emerging chlamydial infections of animals and their zoonotic implications. *Transboundary and Emerging Diseases* 59, 283-91.

Wheelhouse, N., Sait, M., Gidlow, J., Deuchande, R., Borel, N., Baily, J., Caldow, G. and Longbottom, D. (2011). Molecular detection of *Chlamydia*-like organisms in cattle drinking water. *Veterinary Microbiology* 152, 196-9.

Wheelhouse, N., Katzer, F., Wright, F. and Longbottom, D. (2010). Novel *Chlamydia*-like organisms as cause of bovine abortions, UK. *Emerging Infectious Diseases* 16, 1323-1324.

Deuchande, R., Gidlow, J., Caldow, G., Baily, J., Longbottom, D., Wheelhouse, N., Nicole Borel, N. and Greub, G. (2010). *Parachlamydia* involvement in bovine abortions in a beef herd in Scotland. *Veterinary Record* 166, 598-599.